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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,414	09/08/2003	Hamdi K. Hamdi	HAMDI-001C	9021

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EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 01/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/657,414	HAMDI ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-30 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-30 is/are rejected.

7)☒ Claim(s) 8 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 1-30 are pending.

Claims 1-30 are rejected.

Drawings

The drawings are objected to because figures 1-7 are blurry and hard to interpret. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

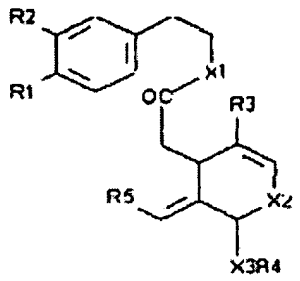
Claim 8 is objected to because of the following informalities: Misspelled inhibiting in the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112-first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating angiogenic condition of wound healing does not reasonably provide enablement for all conditions of angiogenesis with one compound (eg cancers, inflammatory diseases, stroke –these are some of the condition for related angiogenesis). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The term "treating a medical condition which involves angiogenesis" as determined by examiner means to cure



related diseases of angiogenesis with the compound

based upon that, the applicant has not shown any result to convey this. In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The

nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, 7) the relative skill of those skilled in the art and 8) the quantity of experimentation needed.

1) The nature of the invention: Taking for example Stroke-an angiogenesis related disease. In view of the report Express scripts 2003, no treatment can cure stroke (see section How is it treated of the reference). The reference indicates people who suffered from stroke have residual damage.

2) The state of the prior art: There are no examples of how to treat stroke with the above mentioned compound. The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibited the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects.

Thus, in the absence of a showing of correlation between all the diseases claimed as capable of being treated by the compound of the instant claims, one of skill

in the art is unable to fully predict possible results from the administration of the compound due to the unpredictability of the role of the diseases.

3) The predictability or lack thereof in the art: there is currently no completely effective therapy for treating all forms of disease related angiogenesis and definitely no one compound can do all that search for therapeutic agents useful for the treatment of a medical condition which involves angiogenesis. For example: The art pertaining to the treatment of inflammatory conditions remain highly unpredictable. As disclosed above, there is no absolute predictability even in view of the seemingly high level of skill in the art. Firstly, for a compound or genus to be effective against a disease associated with inflammation generally is contrary to medical science. Inflammation is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, leukotrienes, cytokines, and many, many others. Accordingly, treatments for diseases associated with inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against all inflammation related diseases generally. Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilatation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is

infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages that have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters.

Otitis media is an inflammation of the lining of the middle ear and is commonly caused by Streptococcus pneumoniae and Haemophilus influenzae. Cystitis is an inflammation of the bladder, usually caused by bacteria. Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics.

4) The amount of direction or guidance present -The specification only provides examples and no evidence of treating/curing of all cancers in the examples provided, the examples will not enable one skilled in the art to treat all types of cancerous diseases,

5) Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present found on pages 20-26 does not support the claims for treating all medical conditions of angiogenesis.

6) Existence of working examples.

As discussed above, working example is found on pages 20-26 are insufficient for such a broad claim of treatment of all disease of angiogenesis. Applicant's limited

working example does not enable one of ordinary skill in the art to treat the numerous amounts of diseases encompassed by the instant invention.

7) Breadth of claims.

Claim 1 is extremely broad due to the vast number of possible diseases encompassed by the instant invention.

8) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the treatment of all (angiogenesis) disease. As a result necessitating one of skill in the art to perform an exhaustive search to determine which diseases can be treated by the compound(s) of the instant claims in order to practice the claimed invention.

Genentec Inc. V. *Novo Nordisk A/S* (CAFC) 42 USPQ 2D 1001, states that:

"a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds encompassed in instant claims, with no assurance of success.

The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms, and treatment (or lack thereof) for inflammation/stroke.

II. Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for lung, colon, larynx, pancreas, stomach, liver, lung, breast, skin, prostate, ovary, cervix, uterus and bladder cancers does not reasonably provide enablement for all types of cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The term treating as determined by examiner means to cure, based upon that, the applicant has not shown any result to convey this.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, 7) the relative skill of those skilled in the art and 8) the quantity of experimentation needed.

1) The nature of the invention: The method of use claims are drawn to treating cancer but in view of the report by Daniel DeNoon WebMD cancer is not curable, at most will become manageable within a decade as a chronic diseases (see enclosed report). Even though some cancers are curable not all cancer are curable, (see also bottom section of the report) indicates that the for example patients suffering from

metastic colon cancer that took Avastin (an angiogenesis inhibitor) survived for an extra 5 months and that is not a cure.

2) The state of the prior art: The data (see report Daniel DeNoon WebMD) suggests that preventing treating requires an undue amount of research to successfully attain that goal. "there is currently no completely effective therapy for treating all types of cancerous disease. A search for therapeutic agents useful for the treatment of cancer is ongoing".

3) The predictability or lack thereof in the art: there is currently no completely effective therapy for prevention of allergic disease. A search for therapeutic agents useful for the treatment of allergic disease is ongoing.

4) The amount of direction or guidance present -The specification only provides examples and no evidence of treating/curing of all cancers in the examples provided, the examples will not enable one skilled in the art to treat all types of cancerous diseases, 5) the presence or absence of working examples: there is no apparent guidance as to what to expect or how to extrapolate from treating/inhibiting to from the few examples given in the specification.

6) The breadth of the claims: The claims are drawn to methods of treating.

7) The quantity of experimentation needed would be an undue burden since there is inadequate guidance given to the skilled artisan for the reasons stated above.

8) The relative skill of those skilled in the art. Based on the unpredictable nature of the invention, one skilled in the art would not have envisioned practicing the invention without the exercise of undue experimentation burden.

Further, both the treatment of cancer and or inhibition of angiogenesis in a host are quite unpredictable. For example, it was recently revealed that the drug Endostatin is unlikely to be the kind of across-the-board cancer cure that many had hoped for. Out of the 61 terminally ill patients tested, not one recovery had been seen (MSNBC News Services, "Mixed results on new cancer drug", November 9, 2000). Hence, it would not be predictable that a method drawn to inhibiting angiogenesis would be effective in a host in need thereof- such as a host suffering from cancer. Further, treatment of cancer in general is at most unpredictable, as underscored by Gura (Science, v278, 1997, pp.1041-1042) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. Lastly, with regards to treating cancer, the specification lacks the critical steps necessary in presenting some type of predictable response in a population of hosts deemed necessary to treat all cancers. Reasonable guidance with respect to treating any cancer relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. The essential element towards the validation of a preventive therapeutic

is the ability to test the drug on subjects monitored in advance of clinical cancer and link those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of treatment of the disease is the essence of a valid agent. Further, a valid agent administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease. All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in an unpredictable art such as cancer therapy.

In view of the teachings above, and the lack of guidance and or exemplification in the specification, it would not be predictable that the method would function as contemplated. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 112-second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,2 4, 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear in claims 1 and 7 from the claim language of "involves" treating a medical condition what would have been the medical condition that was treated that was affected by antiangiogenesis.

Claims 2 and 4 are directed to a pharmaceutical composition by default contains a "carrier" or "diluent" or else it would not be a composition thus it is not apparent how claim 2 is further limiting to claim 1.

Claim 8 is indefinite since it is not apparent what is defined by "enhibiting"

Double Patenting

I. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-29 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-29 of prior U.S. Patent No. 6,632,798 B2 ('798). This is a double patenting rejection. The claims are word for word identical with that of the patent '798.

II. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-30 are rejected on the ground of nonstatutory double patenting over claims 1-30 of U. S. Patent No. 6,632,798 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: methods of inhibiting angiogenesis.

Both sets of claims refer to treating a medicinal condition by administering a pharmaceutical composition having anti-angiogenic activity, in the current application (claims 1 - 30) refers to treating a medical condition (vascularization, ocular inflammation diseases) and (claims 1-30) in the patent refers to same. The current application claims are an obvious variation of the copending application claims because:

Both set of claims recite using the same compositions and/or derivatives thereof. See current application claims 1 - 30 and patent claims 1 -30. The compositions recited in claims 1- 30 of the current application are an obvious variation of claims 1- 30 in the patent claims.

In view of the foregoing, the patent application claims and the current application claims are obvious variations.

II. Claims 1-30 are rejected on the ground of nonstatutory double patenting over claims 1-36 of the co-pending application 10712,423. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

Both sets of claims refer to treating a medical condition an angiogenesis related disease in the current application (1-30), and in the copending application–cancer in the (claims 1-36) with the same identical compound. The current application claims

anticipate the copending application claims because cancer is a medical disease/condition that results from angiogenesis.

Both applications recite using the same compositions and/or derivatives thereof. See current application claims 1-30 and copending application claims 1-36. The compositions recited in the claims are anticipatory of each other.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher S. F. Low

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SVG
1/17/06